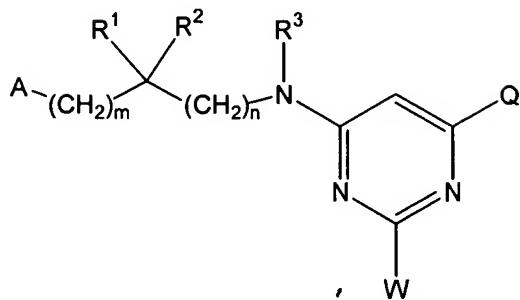


CLAIM AMENDMENTS

1-3. (canceled)

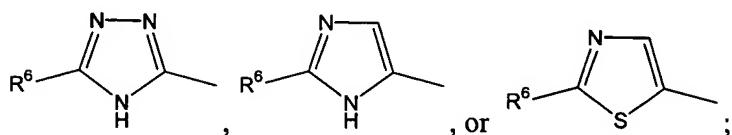
4. (previously amended) A compound of formula



wherein:

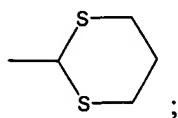
A is A^1 or A^2 ;

A^1 is $R^4R^5N-C(O)-$,



A^2 is chosen from $R^7C(O)NH-$, $R^7S(O)_2NH-$, R^4NH- , and R^4O- ;

Q is chosen from imidazolyl, methylimidazolyl, pyrrolyl, methylpyrrolyl, pyrazolyl, methylpyrazolyl, hydroxymethylimidazolyl, (dimethylaminomethyl)imidazolyl, furanyl, methylfuranyl, thienyl, oxazolyl, thiazolyl, pyridinyl, quinolinyl, 1-methylpyrimidin-2-onyl, phenyl, fluorophenyl, hydroxymethyl, tetrahydropyranoxymethyl, imidazolylmethyl, pyrrolylmethyl, $-CH=N-OCH_3$ and



;

W is chosen from H , Cl , F , R^8 , C_1-C_4 -alkylaryl, $-OR^8$, $-SR^8$, $-NR^9R^{10}$ and $-NHC(O)R^{11}$, with the proviso that when Q is imidazolyl, W is not H , Cl , F or R^8 ;

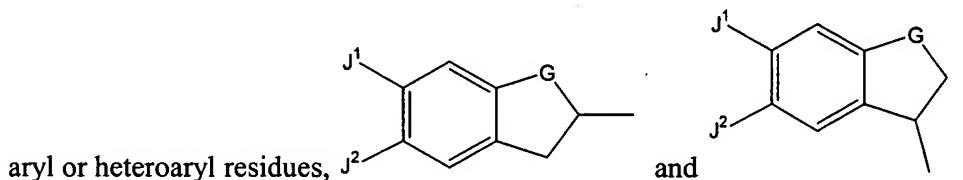
R^1 is chosen from alkyl, cycloalkyl, alkenyl, C_1-C_3 -alkylcycloalkyl, heterocyclyl, C_1-C_3 -alkylheterocyclyl, aryl, C_1-C_3 -alkylaryl, heteroaryl, C_1-C_3 -alkylheteroaryl,

(C₁-C₃-alkyloxy)alkyl, (C₁-C₃-alkyloxy)cycloalkyl, (C₁-C₃-alkylthio)alkyl, (C₁-C₃-alkylthio)cycloalkyl and (C₁-C₃-alkylsulfonyl)alkyl;

R² is H or C₁-C₃-alkyl, or R¹ and R² taken together form a 5- to 7-membered ring structure optionally containing O, S or NR¹²;

R³ is H or C₁-C₆-alkyl, or, when n is zero, R² and R³ taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R⁴ is chosen from H, aryl, heteroaryl, C₁-C₄-alkyl substituted with from one to three



aryl or heteroaryl residues, and , wherein J¹ and J² are independently chosen from H, F, Cl, CN, NO₂ and CH₃, and G is chosen from -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -OCH₂-, -CH₂O-, -CH₂CH₂O-, -OCH₂CH₂-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH₂-, -CH₂N(lower alkyl)-, -S-, -SO-, -SO₂-, -CH₂S-, -SCH₂-, -CH₂SO-, -SOCH₂-, -CH₂SO₂-, and -SO₂CH₂-;

R⁵ is H or C₁-C₃-alkyl, with the proviso that both R³ and R⁵ cannot be alkyl;

R⁶ is aryl;

R⁷ is aryl or C₁-C₃-alkylaryl;

R⁸ is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C₁-C₄-alkylaryl, C₁-C₄-alkylheterocycl and C₁-C₄-alkylheteroaryl;

R⁹ is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C₁-C₄-alkylcycloalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkoxycarbonyl)alkyl, (C₁-C₄-alkylthio)alkyl, heterocycl, C₁-C₄-alkylheterocycl, C₁-C₄-alkylaryl, and C₁-C₄-alkylheteroaryl;

R¹⁰ is H or C₁-C₃-alkyl, or

R⁹ and R¹⁰ taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with -OH, -

CN, -COOH or -COOCH₃;

R¹¹ is aryl;

R¹² is chosen from H, C₁-C₃-alkyl, alkoxy carbonyl, methoxyacetyl and aryl;

m is zero or one; and

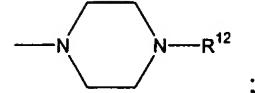
n is zero or one, with the proviso that when A is A², m and n cannot both be zero.

5. (original) A 4-pyrimidinamine according to claim 4 wherein:

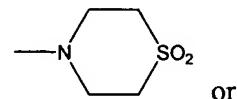
Q is chosen from pyrrol-1-yl, imidazol-1-yl, furan-3-yl, 2-methylimidazol-1-yl and 4-methylimidazol-1-yl;

A is R⁴R⁵N-C(O)-;

W is Cl, NHR⁹, N(CH₃)R⁹, OR⁸, SR⁸, R⁸, morpholin-4-yl,



;



or

R¹ is chosen from alkyl, cycloalkyl, C₁-C₃-alkylaryl, C₁-C₃-alkylcycloalkyl, C₁-C₃-alkylheterocycl, C₁-C₃-alkylheteroaryl;

R², R³ and R⁵ are H;

R⁸ is C₁-C₄-alkylaryl

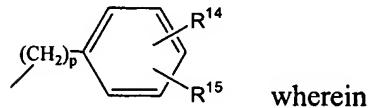
R⁹ is chosen from hydrogen, alkyl, substituted alkyl, (C₁-C₄)-alkoxy, C₁-C₄-alkylcycloalkyl, C₁-C₄-alkylaryl, heterocycl, C₁-C₄-alkylheteroaryl, C₁-C₄-alkylheterocycl; and

m and n are zero.

6. (original) A 4-pyrimidinamine according to claim 5 wherein W is NHR⁹ and

R⁹ is chosen from hydrogen; methyl; ethyl; 2,2,2-trifluoroethyl; allyl; cyclopropyl; 2-cyanoethyl; propargyl; methoxy; methoxyethyl; cyclopropyl; cyclopropylmethyl; (methylthio)ethyl; 3-methoxypropyl; 3-pyridyl; 2-(3-pyridyl)ethyl; 2-(2-pyridyl)ethyl; 3-pyridylmethyl; 4-pyridylmethyl; 4-pyridylmethyl-N-oxide; 2-pyridazinylmethyl; sulfolan-3-yl; 3-tetrahydrofuryl; 2-tetrahydrofurylmethyl; 3-(1-imidazolyl)propyl; 1-t-

butoxycarbonyl-4-piperidinyl; 1-*t*-butoxycarbonyl-4-piperidinylmethyl; 2-(hydroxyimino)propyl; 2-(methoxyimino)propyl; 2-oxo-1-propyl; and

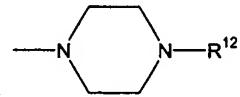


wherein

R¹⁴ is chosen from H, Cl, F, CN, NO₂, SO₂NH₂, CF₃, COOCH₃, OCH₃, OH, SO₂CH₃, N(CH₃)₂ and COOH;

R¹⁵ is chosen from H, OCH₃ and Cl; and

p is 1 or 2.

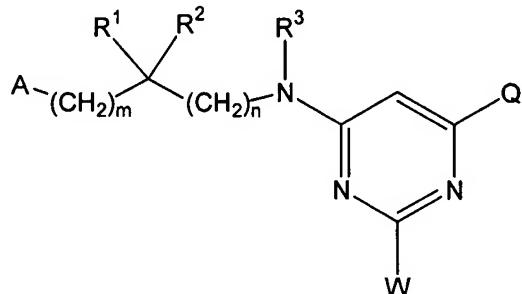


7. (original) A 4-pyrimidinamine according to claim 5 wherein W is

and

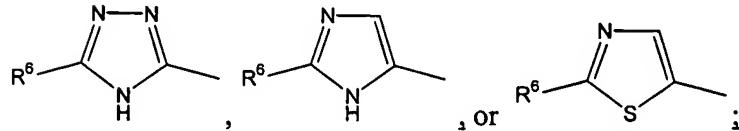
R¹² is *t*-butoxycarbonyl, methoxyacetyl or phenyl.

8. (previously amended) A compound of formula



wherein:

A is



R¹ is chosen from n-butyl; cyclohexylmethyl; cyclopentylmethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-

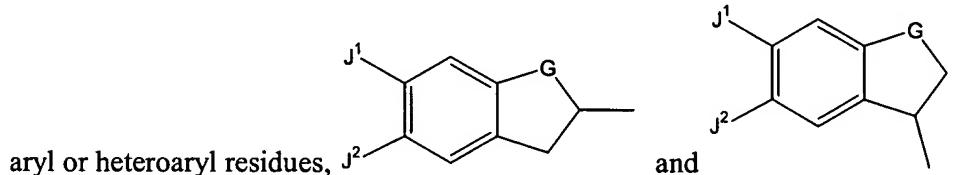
t-butoxycarbonyl-4-piperidinyl; 4-chlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

R² and R³ are H;

Q is imidazolyl or pyrrolyl;

R⁶ is aryl;

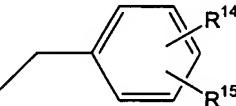
R⁴ is chosen from H, aryl, heteroaryl, C₁-C₄-alkyl substituted with from one to three



aryl or heteroaryl residues, and , wherein J¹ and J² are independently chosen from H, F, Cl, CN, NO₂ and CH₃, and G is chosen from -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -OCH₂-, -CH₂O-, -CH₂CH₂O-, -OCH₂CH₂-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH₂-, -CH₂N(lower alkyl)-, -S-, -SO-, -SO₂-, -CH₂S-, -SCH₂-, -CH₂SO-, -SOCH₂-, -CH₂SO₂-, and -SO₂CH₂;

R⁷ is aryl or C₁-C₃-alkylaryl;

W is NHR⁹; and

R⁹ is alkyl, cycloalkyl or  wherein

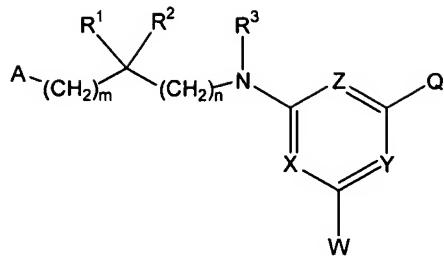
R¹⁴ is chosen from H, Cl, F, CN, NO₂, SO₂NH₂, CF₃, COOCH₃, OCH₃, SO₂CH₃, N(CH₃)₂ and COOH; and

R¹⁵ is chosen from H, OCH₃ and Cl.

m is zero or one; and

n is zero or one, with the proviso that when A is chosen from R⁷C(O)NH-, R⁷S(O)₂NH-, R⁴NH-, and R⁴O-, m and n cannot both be zero.

9. (previously amended) A compound of formula

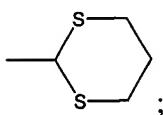


wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

A is $R^4R^5N-C(O)-$;

Q is chosen from heteroaryl, aryl, $-CH_2R^{13}$, $-CH=N-OCH_3$ and

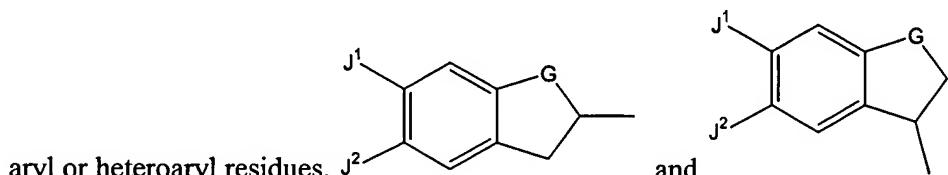


W is chosen from H, Cl, F, R^8 , C_1-C_4 -alkylaryl, $-OR^8$, $-SR^8$, $-NR^9R^{10}$ and $-NHC(O)R^{11}$, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R^8 ;

R^1 is chosen from isopropyl; n-butyl; cyclohexylmethyl; cyclopentylmethyl; naphthylmethyl; cyclohexylethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-t-butoxycarbonyl-4-piperidinyl; 4-methoxybenzyl; 4-chlorobenzyl; 3,4-dichlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

R^2 , R^3 and R^5 are H;

R^4 is chosen from H, aryl, heteroaryl, C_1-C_4 -alkyl substituted with from one to three



aryl or heteroaryl residues, and

, wherein J^1 and J^2 are independently chosen from H, F, Cl, CN, NO_2 and CH_3 , and G is chosen from $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-OCH_2-$, $-CH_2O-$, $-CH_2CH_2O-$, $-OCH_2CH_2-$, $-O-$, $-N(lower\ alkyl)-$, $-N(lower\ alkyl)CH_2-$, $-CH_2N(lower\ alkyl)-$, $-S-$, $-SO-$, $-SO_2-$, $-CH_2S-$, $-SCH_2-$, $-CH_2SO-$, $-SOCH_2-$, $-CH_2SO_2-$, and $-SO_2CH_2-$;

R^7 is aryl or C_1 - C_3 -alkylaryl;

R^8 is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C_1 - C_4 -alkylaryl, C_1 - C_4 -alkylheterocyclyl and C_1 - C_4 -alkylheteroaryl;

R^9 is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C_1 - C_4 -alkylcycloalkyl, (C_1 - C_4 -alkoxy)alkyl, (C_1 - C_4 -alkoxycarbonyl)alkyl, (C_1 - C_4 -alkylthio)alkyl, heterocyclyl, C_1 - C_4 -alkylheterocyclyl, C_1 - C_4 -alkylaryl, and C_1 - C_4 -alkylheteroaryl;

R^{10} is H or C_1 - C_3 -alkyl, or

R^9 and R^{10} taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with -OH, -CN, -COOH or -COOCH₃;

R^{11} is aryl;

R^{12} is chosen from H, C_1 - C_3 -alkyl, alkoxy carbonyl, methoxyacetyl and aryl;

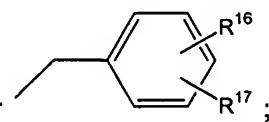
R^{13} is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is chosen from $R^7C(O)NH$ -, $R^7S(O)_2NH$ -, R^4NH -, and R^4O -, m and n cannot both be zero.

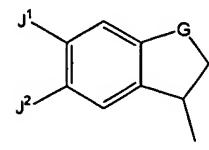
10. (original) A pyrimidine according to claim 9 wherein:

R^4 is pyridinyl, pyridinylmethyl, tetrahydronaphthalenyl, indanyl methyl,

furanylmethyl, substituted phenyl, or ;

R^{16} is chosen from H, Cl, F, CN, NO₂, SO₂NH₂, CF₃, CH₃, COOCH₃, OCH₃, SO₂CH₃, SOCH₃, N(CH₃)₂, tetrazol-5-yl, CONH₂, C(=NOH)NH₂ and COOH; and

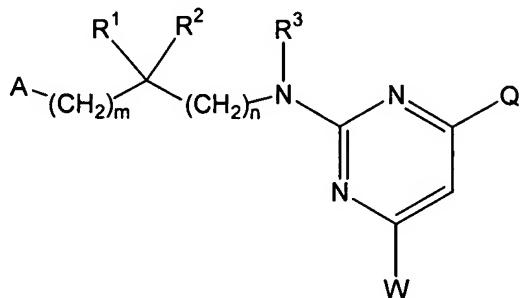
R^{17} is chosen from H, OCH₃, F and Cl.



11. (original) A pyrimidine according to claim 9 wherein R⁴ is

J¹ and J² is H and the other is H, Cl or CN and G is chosen from -CH₂-, -CH₂CH₂-, -OCH₂-, -O- and -CH₂N(lower alkyl)-.

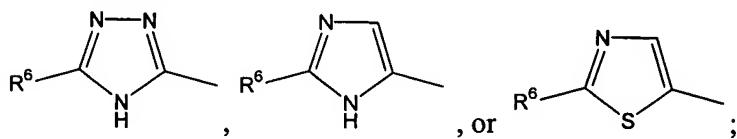
12. (previously amended) A compound of formula



wherein:

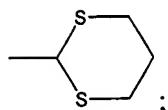
A is A¹ or A²;

A¹ is R⁴R⁵N-C(O)-,



A² is chosen from R⁷C(O)NH-, R⁷S(O)₂NH-, R⁴NH-, and R⁴O-;

Q is chosen from heteroaryl, aryl, -CH₂R¹³, -CH=N-OCH₃ and



W is chosen from H, Cl, F, R⁸, C₁-C₄-alkylaryl, -OR⁸, -SR⁸, -NR⁹R¹⁰ and -

NHC(O)R¹¹, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R⁸;

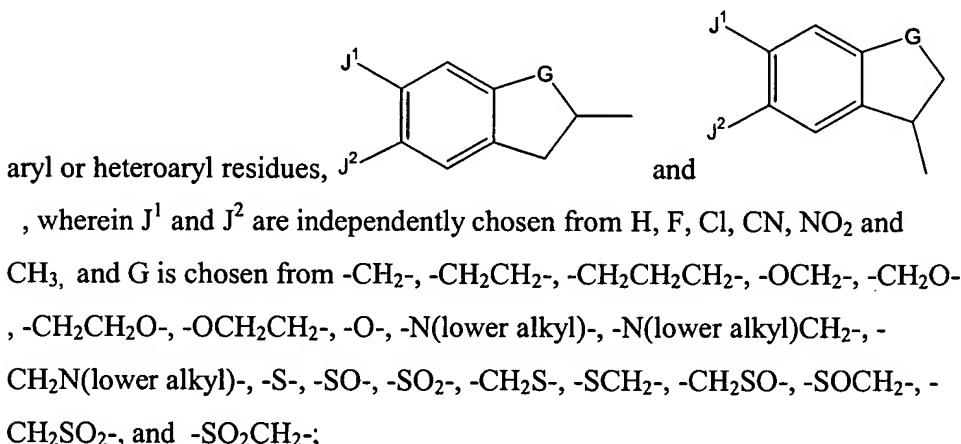
R¹ is chosen from alkyl, cycloalkyl, alkenyl, C₁-C₃-alkylcycloalkyl, heterocyclyl, C₁-C₃-alkylheterocyclyl, aryl, C₁-C₃-alkylaryl, heteroaryl, C₁-C₃-alkylheteroaryl,

(C₁-C₃-alkyloxy)alkyl, (C₁-C₃-alkyloxy)cycloalkyl, (C₁-C₃-alkylthio)alkyl, (C₁-C₃-alkylthio)cycloalkyl and (C₁-C₃-alkylsulfonyl)alkyl;

R² is H or C₁-C₃-alkyl, or R¹ and R² taken together form a 5- to 7-membered ring structure optionally containing O, S or NR¹²;

R³ is H or C₁-C₆-alkyl, or, when n is zero, R² and R³ taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R⁴ is chosen from H, aryl, heteroaryl, C₁-C₄-alkyl substituted with from one to three



R⁵ is H or C₁-C₃-alkyl, with the proviso that both R³ and R⁵ cannot be alkyl;

R⁶ is aryl;

R⁷ is aryl or C₁-C₃-alkylaryl;

R⁸ is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C₁-C₄-alkylaryl, C₁-C₄-alkylheterocycl and C₁-C₄-alkylheteroaryl;

R⁹ is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C₁-C₄-alkylcycloalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkoxycarbonyl)alkyl, (C₁-C₄-alkylthio)alkyl, heterocycl, C₁-C₄-alkylheterocycl, C₁-C₄-alkylaryl, and C₁-C₄-alkylheteroaryl;

R¹⁰ is H or C₁-C₃-alkyl, or

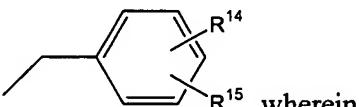
R⁹ and R¹⁰ taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with -OH, -CN, -COOH or -COOCH₃;

R^{11} is aryl;
 R^{12} is chosen from H, C₁-C₃-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;
 R^{13} is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;
 m is zero or one; and
 n is zero or one, with the proviso that when A is A², m and n cannot both be zero.

13. (previously amended) A 2-pyrimidinamine according to claim 12 wherein Q is chosen from imidazolyl, pyrrolyl, pyridinyl, fluorophenyl and 2-thienyl.

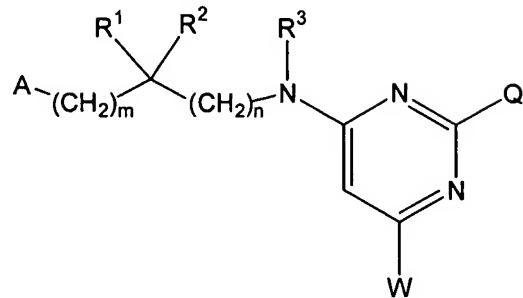
14. (original) A 2-pyrimidinamine according to claim 13 wherein
 A is $R^4R^5N-C(O)-$;
 W is H, Cl, NHR⁹ or OR⁸;
 R^1 is chosen from alkyl and C₁-C₃-alkylcycloalkyl;
 R^2 , R^3 and R^5 are H;
 R^4 is C₁-C₄-alkylaryl or C₁-C₄-alkylheteroaryl;
 R^8 is C₁-C₄-alkylaryl;
 R^9 is chosen from hydrogen, alkyl, fluoroalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkylthio)alkyl, C₁-C₄-alkylcycloalkyl, C₁-C₄-alkylaryl, heterocyclyl, C₁-C₄-alkylheteroaryl, C₁-C₄-alkylheterocyclyl; and
 m and n are zero.

15. (original) A 2-pyrimidinamine according to claim 14 wherein W is NHR⁹ and

R^9 is  wherein
 R^{14} is chosen from H, F, Cl, CN, NO₂, SO₂NH₂, CF₃, COOCH₃, OCH₃, SO₂CH₃, N(CH₃)₂ and COOH; and
 R^{15} is chosen from H, OCH₃ and Cl.

16-17. (canceled)

18. (previously amended) A compound of formula



wherein:

A is R⁴R⁵N-C(O)-;

Q is chosen from imidazolyl and pyrrolyl;

W is NHR⁹;

R¹ is chosen from cyclohexylmethyl; 2-methylpropyl and 3-methyl-1-butyl;

R², R³ and R⁵ are H;

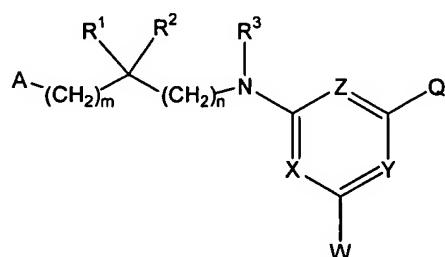
R⁴ and R⁹ are benzyl or substituted benzyl;

m is zero; and

n is zero.

19-25. (canceled)

26. (previously amended) A compound of formula

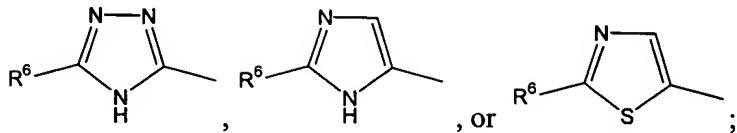


wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

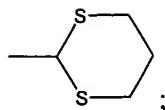
A is A¹ or A²;

A^1 is $R^4R^5N-C(O)-$,



A^2 is chosen from $R^7C(O)NH-$, $R^7S(O)_2NH-$, R^4NH- , and R^4O- ;

Q is chosen from heteroaryl, aryl, $-CH_2R^{13}$, $-CH=N-OCH_3$ and

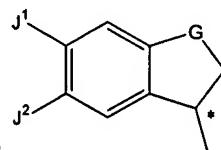


W is chosen from H, Cl, F, R^8 , C_1 - C_4 -alkylaryl, $-OR^8$, $-SR^8$, $-NR^9R^{10}$ and $-NHC(O)R^{11}$, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R^8 ;

R^1 is chosen from alkyl, cycloalkyl, alkenyl, C_1 - C_3 -alkylcycloalkyl, heterocyclyl, C_1 - C_3 -alkylheterocyclyl, aryl, C_1 - C_3 -alkylaryl, heteroaryl, C_1 - C_3 -alkylheteroaryl, (C_1 - C_3 -alkyloxy)alkyl, (C_1 - C_3 -alkyloxy)cycloalkyl, (C_1 - C_3 -alkylthio)alkyl, (C_1 - C_3 -alkylthio)cycloalkyl and (C_1 - C_3 -alkylsulfonyl)alkyl;

R^2 is H or C_1 - C_3 -alkyl, or R^1 and R^2 taken together form a 5- to 7-membered ring structure optionally containing O, S or NR^{12} ;

R^3 is H or C_1 - C_6 -alkyl, or, when n is zero, R^2 and R^3 taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;



R^4 is is having the R configuration at the carbon indicated with an asterisk, wherein J^1 and J^2 are independently chosen from H, F, Cl, CN, NO_2 and CH_3 , and G is chosen from $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-OCH_2-$, $-CH_2O-$, $-CH_2CH_2O-$, $-OCH_2CH_2-$, $-O-$, $-N(lower\ alkyl)-$, $-N(lower\ alkyl)CH_2-$, $-CH_2N(lower\ alkyl)-$, $-S-$, $-SO-$, $-SO_2-$, $-CH_2S-$, $-SCH_2-$, $-CH_2SO-$, $-SOCH_2-$, $-CH_2SO_2-$, and $-SO_2CH_2-$;

R^5 is H or C_1 - C_3 -alkyl, with the proviso that both R^3 and R^5 cannot be alkyl;

R^6 is aryl;

R⁷ is aryl or C₁-C₃-alkylaryl;

R⁸ is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C₁-C₄-alkylaryl, C₁-C₄-alkylheterocyclyl and C₁-C₄-alkylheteroaryl;

R⁹ is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C₁-C₄-alkylcycloalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkoxycarbonyl)alkyl, (C₁-C₄-alkylthio)alkyl, heterocyclyl, C₁-C₄-alkylheterocyclyl, C₁-C₄-alkylaryl, and C₁-C₄-alkylheteroaryl;

R¹⁰ is H or C₁-C₃-alkyl, or

R⁹ and R¹⁰ taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with -OH, -CN, -COOH or -COOCH₃;

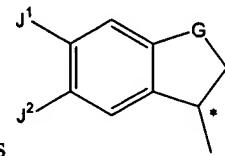
R¹¹ is aryl;

R¹² is chosen from H, C₁-C₃-alkyl, alkoxy carbonyl, methoxyacetyl and aryl;

R¹³ is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

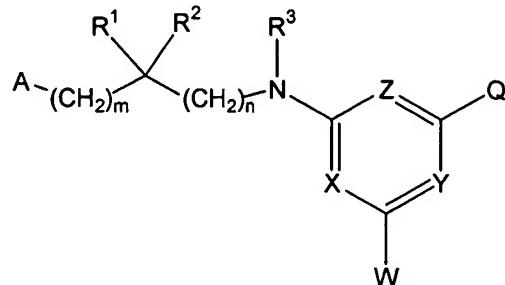
m is zero or one; and

n is zero or one, with the proviso that when A is A², m and n cannot both be zero.



27. (original) A pyrimidine according to claim 12 wherein R⁴ is having the R configuration at the carbon indicated with an asterisk.

28. (previously amended) A compound of formula

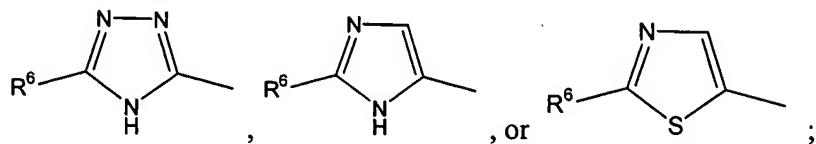


wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

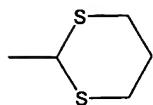
A is A¹ or A²;

A¹ is R⁴R⁵N-C(O)-,



A² is chosen from R⁷C(O)NH-, R⁷S(O)₂NH-, R⁴NH-, and R⁴O-;

Q is chosen from aryl, -CH₂R¹³, -CH=N-OCH₃ and



heteroaryl other than 1-imidazolyl and 1-triazolyl;

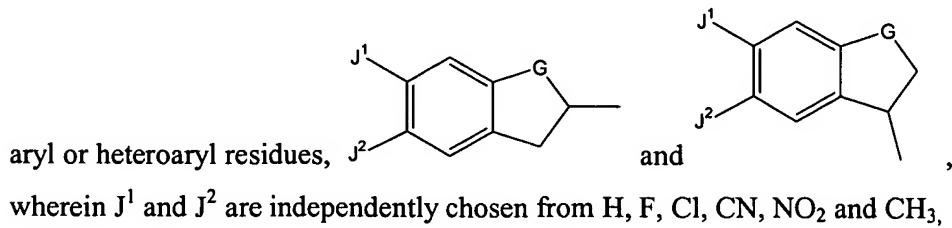
W is chosen from H, Cl, F, R⁸, C₁-C₄-alkylaryl, -OR⁸, -SR⁸, -NR⁹R¹⁰ and -NHC(O)R¹¹, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R⁸;

R¹ is chosen from alkyl, cycloalkyl, alkenyl, C₁-C₃-alkylcycloalkyl, heterocyclyl, C₁-C₃-alkylheterocyclyl, aryl, C₁-C₃-alkylaryl, heteroaryl, C₁-C₃-alkylheteroaryl, (C₁-C₃-alkyloxy)alkyl, (C₁-C₃-alkyloxy)cycloalkyl, (C₁-C₃-alkylthio)alkyl, (C₁-C₃-alkylthio)cycloalkyl and (C₁-C₃-alkylsulfonyl)alkyl;

R² is H or C₁-C₃-alkyl, or R¹ and R² taken together form a 5- to 7-membered ring structure optionally containing O, S or NR¹²;

R³ is H or C₁-C₆-alkyl, or, when n is zero, R² and R³ taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R⁴ is chosen from H, aryl, heteroaryl, C₁-C₄-alkyl substituted with from one to three



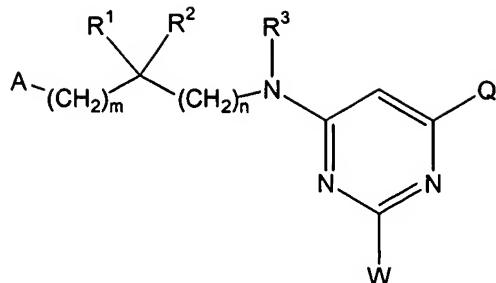
and G is chosen from -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -OCH₂-, -CH₂O-, -CH₂CH₂O-, -OCH₂CH₂-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH₂-, -

CH₂N(lower alkyl)-, -S-, -SO-, -SO₂-, -CH₂S-, -SCH₂-, -CH₂SO-, -SOCH₂-, -CH₂SO₂-, and -SO₂CH₂-;

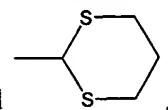
R⁵ is H or C₁-C₃-alkyl, with the proviso that both R³ and R⁵ cannot be alkyl;
R⁶ is aryl;
R⁷ is aryl or C₁-C₃-alkylaryl;
R⁸ is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C₁-C₄-alkylaryl, C₁-C₄-alkylheterocycl and C₁-C₄-alkylheteroaryl;
R⁹ is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C₁-C₄-alkylcycloalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkoxycarbonyl)alkyl, (C₁-C₄-alkylthio)alkyl, heterocycl, C₁-C₄-alkylheterocycl, C₁-C₄-alkylaryl, and C₁-C₄-alkylheteroaryl;
R¹⁰ is H or C₁-C₃-alkyl, or
R⁹ and R¹⁰ taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with -OH, -CN, -COOH or -COOCH₃;
R¹¹ is aryl;
R¹² is chosen from H, C₁-C₃-alkyl, alkoxy carbonyl, methoxyacetyl and aryl;
R¹³ is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;
m is zero or one; and
n is zero or one, with the proviso that when A is A², m and n cannot both be zero.

29. (canceled)

30. (previously amended) A 4-pyrimidinamine according to claim 28, wherein Z is CH, having the formula



31. (original) A 4-pyrimidinamine according to claim 30 wherein Q is chosen from methylimidazolyl, pyrrolyl, methylpyrrolyl, pyrazolyl, methylpyrazolyl, furanyl, methylfuranyl, thienyl, oxazolyl, thiazolyl, pyridinyl, quinolinyl, 1-methylpyrimidin-2-onyl, phenyl, fluorophenyl, hydroxymethyl, 2-imidazolyl, tetrahydropyranloxyethyl, imidazolylmethyl, pyrrolylmethyl, -CH=N-OCH₃ and

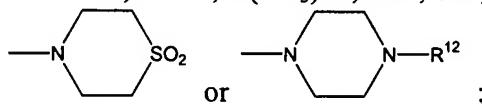


32. (original) A 4-pyrimidinamine according to claim 31 wherein:

Q is chosen from pyrrol-1-yl, imidazol-1-yl, furan-3-yl, 2-methylimidazol-1-yl and 4-methylimidazol-1-yl;

A is R⁴R⁵N-C(O)-;

W is Cl, NHR⁹, N(CH₃)R⁹, OR⁸, SR⁸, R⁸, morpholin-4-yl,



R¹ is chosen from alkyl, cycloalkyl, C₁-C₃-alkylaryl, C₁-C₃-alkylcycloalkyl, C₁-C₃-alkylheterocyclyl, C₁-C₃-alkylheteroaryl ;

R², R³ and R⁵ are H;

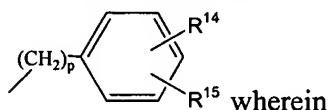
R⁸ is C₁-C₄-alkylaryl

R⁹ is chosen from hydrogen, alkyl, substituted alkyl, (C₁-C₄)-alkoxy, C₁-C₄-alkylcycloalkyl, C₁-C₄-alkylaryl, heterocyclyl, C₁-C₄-alkylheteroaryl, C₁-C₄-alkylheterocyclyl; and

m and n are zero.

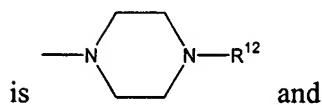
33. (original) A 4-pyrimidinamine according to claim 32 wherein W is NHR⁹ and

R⁹ is chosen from hydrogen; methyl; ethyl; 2,2,2-trifluoroethyl; allyl; cyclopropyl; 2-cyanoethyl; propargyl; methoxy; methoxyethyl; cyclopropyl; cyclopropylmethyl; (methylthio)ethyl; 3-methoxypropyl; 3-pyridyl; 2-(3-pyridyl)ethyl; 2-(2-pyridyl)ethyl; 3-pyridylmethyl; 4-pyridylmethyl; 4-pyridylmethyl-N-oxide; 2-pyridazinylmethyl; sulfolan-3-yl; 3-tetrahydrofuranyl; 2-tetrahydrofuranylmethyl; 3-(1-imidazolyl)propyl; 1-t-butoxycarbonyl-4-piperidinyl; 1-t-butoxycarbonyl-4-piperidinylmethyl; 2-(hydroxyimino)propyl; 2-(methoxyimino)propyl; 2-oxo-1-propyl; and



R¹⁴ is chosen from H, Cl, F, CN, NO₂, SO₂NH₂, CF₃, COOCH₃, OCH₃, OH, SO₂CH₃, N(CH₃)₂ and COOH;
R¹⁵ is chosen from H, OCH₃ and Cl; and
p is 1 or 2.

34. (original) A 4-pyrimidinamine according to claim 32 wherein W

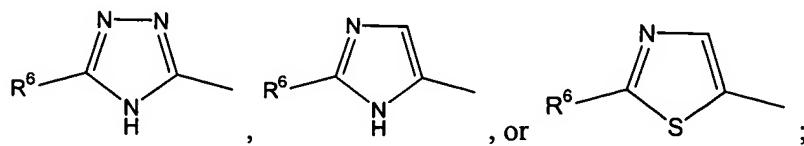


is and
R¹² is t-butoxycarbonyl, methoxyacetyl or phenyl.

35. (previously amended) A 4-pyrimidinamine according to claim 28 wherein

Z is CH;

A is



R¹ is chosen from n-butyl; cyclohexylmethyl; cyclopentylmethyl; 2-methylpropyl;

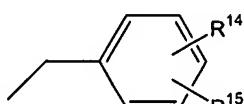
3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-

t-butoxycarbonyl-4-piperidinyl; 4-chlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

R² and R³ are H;

Q is pyrrolyl;

W is NHR⁹; and

R⁹ is alkyl, cycloalkyl or  wherein
R¹⁴ is chosen from H, Cl, F, CN, NO₂, SO₂NH₂, CF₃, COOCH₃, OCH₃, SO₂CH₃, N(CH₃)₂ and COOH; and
R¹⁵ is chosen from H, OCH₃ and Cl.

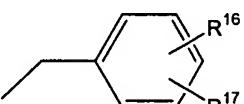
36. (previously amended) A pyrimidine according to claim 28 wherein:

A is R⁴R⁵N-C(O)-;

R¹ is chosen from isopropyl; n-butyl; cyclohexylmethyl; cyclopentylmethyl; naphthylmethyl; cyclohexylethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-*t*-butoxycarbonyl-4-piperidinyl; 4-methoxybenzyl; 4-chlorobenzyl; 3,4-dichlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

R², R³ and R⁵ are H;

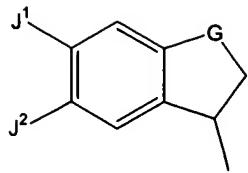
R⁴ is pyridinyl, pyridinylmethyl, indanylmethyl, furanylmethyl, tetrahydronaphthalenyl,

substituted phenyl, or ;

R¹⁶ is chosen from H, Cl, F, CN, NO₂, SO₂NH₂, CF₃, CH₃, COOCH₃, OCH₃, SO₂CH₃, N(CH₃)₂ and COOH; and

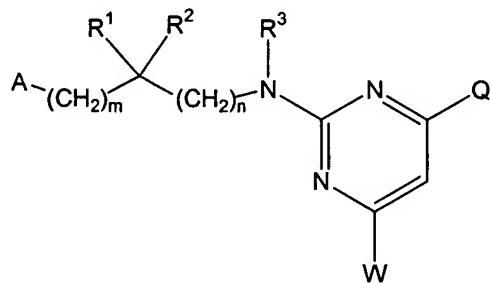
R¹⁷ is chosen from H, OCH₃, F and Cl.

37. (previously amended) A pyrimidine according to claim 28 wherein R⁴ is



38. (original) A pyrimidine according to claim 37 wherein one of J¹ and J² is H and the other is H, Cl or CN and G is chosen from -CH₂-, -CH₂CH₂-, -OCH₂-, -O- and -CH₂N(lower alkyl)-.

39. (previously amended) A 2-pyrimidinamine according to claim 28, wherein Y is CH, having the formula



40. (original) A 2-pyrimidinamine according to claim 39 wherein Q is chosen from pyrrolyl, pyridinyl, fluorophenyl and 2-thienyl.

41. (original) A 2-pyrimidinamine according to claim 40 wherein

A is R⁴R⁵N-C(O)-;

W is H, Cl, NHR⁹ or OR⁸;

R¹ is chosen from alkyl and C₁-C₃-alkylcycloalkyl;

R², R³ and R⁵ are H;

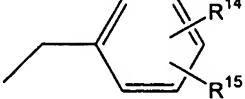
R⁴ is C₁-C₄-alkylaryl or C₁-C₄-alkylheteroaryl;

R⁸ is C₁-C₄-alkylaryl;

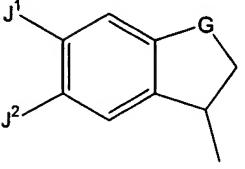
R⁹ is chosen from hydrogen, alkyl, fluoroalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkylthio)alkyl, C₁-C₄-alkylcycloalkyl, C₁-C₄-alkylaryl, heterocyclyl, C₁-C₄-alkylheteroaryl, C₁-C₄-alkylheterocyclyl; and

m and n are zero.

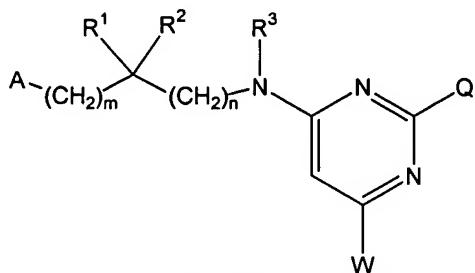
42. (original) A 2-pyrimidinamine according to claim 41 wherein W is NHR⁹ and

R⁹ is  wherein
R¹⁴ is chosen from H, F, Cl, CN, NO₂, SO₂NH₂, CF₃, COOCH₃, OCH₃, SO₂CH₃, N(CH₃)₂ and COOH; and
R¹⁵ is chosen from H, OCH₃ and Cl.

43. (original) A 2-pyrimidineamine according to claim 39 wherein R⁴ is

 , one of J¹ and J² is H and the other is H, Cl or CN and G is chosen from -CH₂-, -CH₂CH₂-, -OCH₂-, -O- and -CH₂N(lower alkyl)-.

44. (previously amended) A 4-pyrimidinamine according to claim 28, wherein X is CH, having the formula



45. (original) A 4-pyrimidinamine according to claim 44 wherein Q is pyrrolyl and m and n are zero.

46. (original) A 4-pyrimidinamine according to claim 45 wherein:

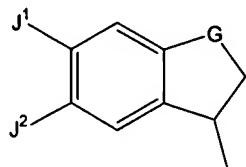
A is R⁴R⁵N-C(O)-;
W is NHR⁹;

R^1 is chosen from cyclohexylmethyl; 2-methylpropyl and 3-methyl-1-butyl;

R^2 , R^3 and R^5 are H; and

R^4 and R^9 are benzyl or substituted benzyl.

47. (original) A 4-pyrimidineamine according to claim 44 wherein R^4 is



, one of J^1 and J^2 is H and the other is H, Cl or CN and G is chosen from - CH_2 -, - CH_2CH_2 -, - OCH_2 -, -O- and - CH_2N (lower alkyl)-.

48. (previously amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to any of claims 4, 9, 12, or 26.

49. (original) A pharmaceutical composition according to claim 48 additionally comprising a steroidal or nonsteroidal antiinflammatory drug (NSAID).

50-51. (canceled)

52. (original) A pharmaceutical composition according to claim 48 additionally comprising a cyclooxygenase inhibitor.

53. (canceled)

54. (original) A pharmaceutical composition according to claim 48 additionally comprising a selective cyclooxygenase-2 inhibitor.

55. (canceled)

56. (original) A pharmaceutical composition according to claim 48 additionally

comprising a selective cyclooxygenase-1 inhibitor.

57-58. (canceled)

59. (original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 28.

60. (original) A pharmaceutical composition according to claim 59 additionally comprising a steroidal or nonsteroidal antiinflammatory drug (NSAID).

61. (original) A pharmaceutical composition according to claim 59 additionally comprising a nonsteroidal antiinflammatory drug (NSAID).

62. (original) A pharmaceutical composition according to claim 61 wherein said NSAID is chosen from arylpropionic acids, arylacetic acids, arylbutyric acids, fenamic acids, arylcarboxylic acids, pyrazoles, pyrazolones, salicylic acids; and oxicams.

63. (original) A pharmaceutical composition according to claim 59 additionally comprising a cyclooxygenase inhibitor.

64. (original) A pharmaceutical composition according to claim 63 wherein said cyclooxygenase inhibitor is ibuprofen or a salicylic acid derivative.

65. (original) A pharmaceutical composition according to claim 59 additionally comprising a selective cyclooxygenase-2 inhibitor.

66. (original) A pharmaceutical composition according to claim 65 wherein said selective cyclooxygenase-2 inhibitor is rofecoxib or celecoxib.

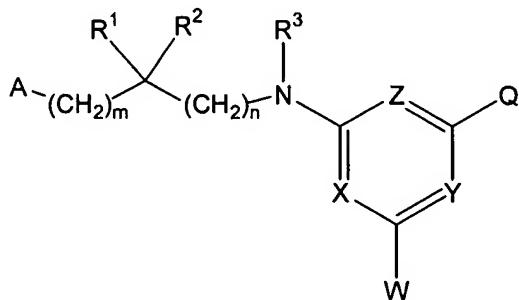
67. (original) A pharmaceutical composition according to claim 59 additionally

comprising a selective cyclooxygenase-1 inhibitor.

68. (original) A pharmaceutical composition according to claim 59 additionally comprising a steroidal antiinflammatory drug.

69. (original) A pharmaceutical composition according to claim 68 wherein said steroidal antiinflammatory drug is chosen from finasteride, beclomethasone and hydrocortisone.

70. (previously amended) A method of treating vasculopathy comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I



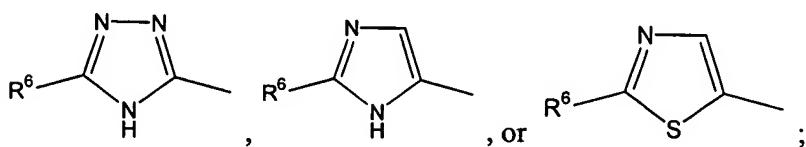
I

wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

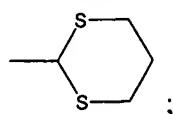
A is A^1 or A^2 ;

A^1 is $R^4R^5N-C(O)-$,



A^2 is chosen from $R^7C(O)NH-$, $R^7S(O)_2NH-$, R^4NH- , and R^4O- ;

Q is chosen from heteroaryl, aryl, $-CH_2R^{13}$, $-CH=N-OCH_3$ and



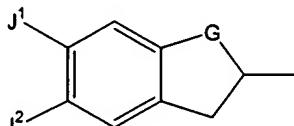
W is chosen from H, Cl, F, R⁸, C₁-C₄-alkylaryl, -OR⁸, -SR⁸, -NR⁹R¹⁰ and -NHC(O)R¹¹, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R⁸;

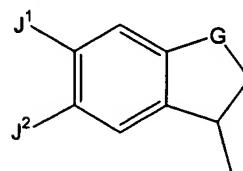
R¹ is chosen from alkyl, cycloalkyl, alkenyl, C₁-C₃-alkylcycloalkyl, heterocycl, C₁-C₃-alkylheterocycl, aryl, C₁-C₃-alkylaryl, heteroaryl, C₁-C₃-alkylheteroaryl, (C₁-C₃-alkyloxy)alkyl, (C₁-C₃-alkyloxy)cycloalkyl, (C₁-C₃-alkylthio)alkyl, (C₁-C₃-alkylthio)cycloalkyl and (C₁-C₃-alkylsulfonyl)alkyl;

R² is H or C₁-C₃-alkyl, or R¹ and R² taken together form a 5- to 7-membered ring structure optionally containing O, S or NR¹²;

R³ is H or C₁-C₆-alkyl, or, when n is zero, R² and R³ taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R⁴ is chosen from H, aryl, heteroaryl, C₁-C₄-alkyl substituted with from one to

three aryl or heteroaryl residues,  and



, wherein J¹ and J² are independently chosen from H, F, Cl, CN, NO₂ and CH₃, and G is chosen from -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -OCH₂-, -CH₂O-, -CH₂CH₂O-, -OCH₂CH₂-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH₂-, -CH₂N(lower alkyl)-, -S-, -SO-, -SO₂-, -CH₂S-, -SCH₂-, -CH₂SO-, -SOCH₂-, -CH₂SO₂-, and -SO₂CH₂-;

R⁵ is H or C₁-C₃-alkyl, with the proviso that both R³ and R⁵ cannot be alkyl;

R⁶ is aryl;

R⁷ is aryl or C₁-C₃-alkylaryl;

R⁸ is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C₁-C₄-alkylaryl, C₁-C₄-alkylheterocycl and C₁-C₄-alkylheteroaryl;

R⁹ is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C₁-C₄-alkylcycloalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkoxycarbonyl)alkyl, (C₁-C₄-alkylthio)alkyl, heterocyclyl, C₁-C₄-alkylheterocyclyl, C₁-C₄-alkylaryl, and C₁-C₄-alkylheteroaryl;

R¹⁰ is H or C₁-C₃-alkyl, or

R⁹ and R¹⁰ taken together may form a 5- to 7-membered ring structure optionally

containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with -OH, -CN, -COOH or -COOCH₃;

R¹¹ is aryl;

R¹² is chosen from H, C₁-C₃-alkyl, alkoxy carbonyl, methoxyacetyl and aryl;

R¹³ is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is A², m and n cannot both be zero.

71. (canceled)

72. (previously amended) The method according to claim 70 wherein said vasculopathy is diabetic vasculopathy.

73. (previously amended) The method according to claim 100 wherein said diabetic symptoms associated with insulitis comprise hyperglycemia, diuresis, proteinuria and increased nitrile and kallikrein urinary excretion.

74-75. (canceled)

76. (previously amended) The method according to claim 99 wherein said pain is chronic pain, pain associated with inflammation or dental pain.

77. (previously amended) The method of treating pain or hyperalgesia according to claim 99 additionally comprising administering a steroid or nonsteroidal antiinflammatory drug (NSAID).

78. (original) The method of treating pain or hyperalgesia according to claim 77 wherein an NSAID is administered.

79. (previously amended) The method of treating pain or hyperalgesia according to claim 99 additionally comprising administering a cyclooxygenase inhibitor.

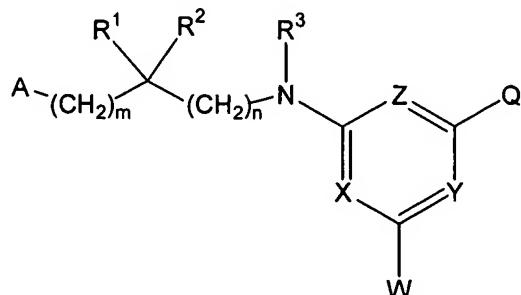
80. (original) The method of treating pain or hyperalgesia according to claim 79 wherein said cyclooxygenase inhibitor is a selective cyclooxygenase-2 inhibitor.

81. (original) The method of treating pain or hyperalgesia according to claim 79 wherein said cyclooxygenase inhibitor is a selective cyclooxygenase-1 inhibitor.

82-94. (canceled)

95. (previously added) The method according to claim 70 wherein said vasculopathy is hypertensive vasculopathy.

96. (previously added) A method of treating asthma comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I



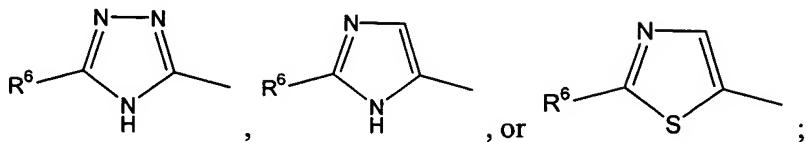
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wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

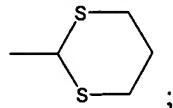
A is A¹ or A²;

A¹ is R⁴R⁵N-C(O)-,



A² is chosen from R⁷C(O)NH-, R⁷S(O)₂NH-, R⁴NH-, and R⁴O-;

Q is chosen from heteroaryl, aryl, -CH₂R¹³, -CH=N-OCH₃ and



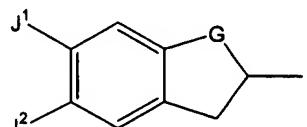
W is chosen from H, Cl, F, R⁸, C₁-C₄-alkylaryl, -OR⁸, -SR⁸, -NR⁹R¹⁰ and -NHC(O)R¹¹, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R⁸;

R¹ is chosen from alkyl, cycloalkyl, alkenyl, C₁-C₃-alkylcycloalkyl, heterocycl, C₁-C₃-alkylheterocycl, aryl, C₁-C₃-alkylaryl, heteroaryl, C₁-C₃-alkylheteroaryl, (C₁-C₃-alkyloxy)alkyl, (C₁-C₃-alkyloxy)cycloalkyl, (C₁-C₃-alkylthio)alkyl, (C₁-C₃-alkylthio)cycloalkyl and (C₁-C₃-alkylsulfonyl)alkyl;

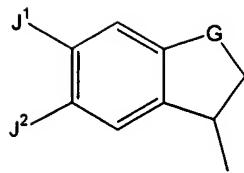
R² is H or C₁-C₃-alkyl, or R¹ and R² taken together form a 5- to 7-membered ring structure optionally containing O, S or NR¹²;

R³ is H or C₁-C₆-alkyl, or, when n is zero, R² and R³ taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R⁴ is chosen from H, aryl, heteroaryl, C₁-C₄-alkyl substituted with from one to



three aryl or heteroaryl residues, and



, wherein J¹ and J² are independently chosen from H,

F, Cl, CN, NO₂ and CH₃, and G is chosen from -CH₂-, -CH₂CH₂-,
-CH₂CH₂CH₂-, -OCH₂-, -CH₂O-, -CH₂CH₂O-, -OCH₂CH₂-, -O-, -N(lower
alkyl)-, -N(lower alkyl)CH₂-, -CH₂N(lower alkyl)-, -S-, -SO-, -SO₂-,
-CH₂S-, -SCH₂-, -CH₂SO-, -SOCH₂-, -CH₂SO₂-, and -SO₂CH₂-;

R⁵ is H or C₁-C₃-alkyl, with the proviso that both R³ and R⁵ cannot be alkyl;

R⁶ is aryl;

R⁷ is aryl or C₁-C₃-alkylaryl;

R⁸ is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C₁-C₄-alkylaryl, C₁-
C₄-alkylheterocycl and C₁-C₄-alkylheteroaryl;

R⁹ is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy,
heteroaryl, fluoroalkyl, C₁-C₄-alkylcycloalkyl, (C₁-C₄-alkoxy)alkyl,
(C₁-C₄-alkoxycarbonyl)alkyl, (C₁-C₄-alkylthio)alkyl, heterocycl, C₁-
C₄-alkylheterocycl, C₁-C₄-alkylaryl, and C₁-C₄-alkylheteroaryl;

R¹⁰ is H or C₁-C₃-alkyl, or

R⁹ and R¹⁰ taken together may form a 5- to 7-membered ring structure optionally

containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with
-OH, -CN, -COOH or -COOCH₃;

R¹¹ is aryl;

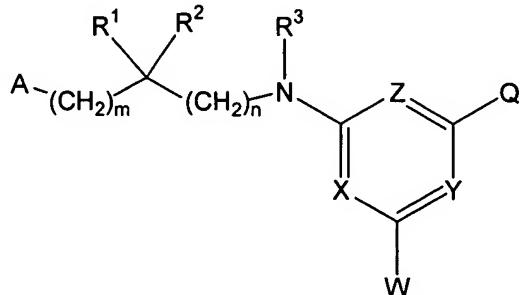
R¹² is chosen from H, C₁-C₃-alkyl, alkoxy carbonyl, methoxyacetyl and aryl;

R¹³ is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is A², m and n cannot both be
zero.

99. (previously added) A method of treating pain or hyperalgesia comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I



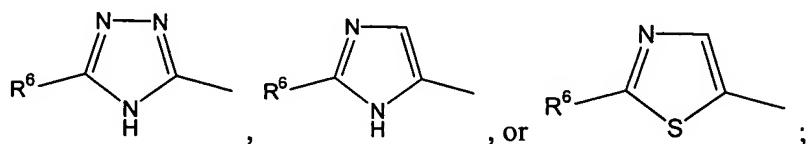
I

wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

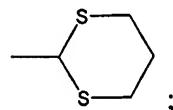
A is A¹ or A²;

A¹ is R⁴R⁵N-C(O)-,



A² is chosen from R⁷C(O)NH-, R⁷S(O)₂NH-, R⁴NH-, and R⁴O-;

Q is chosen from heteroaryl, aryl, -CH₂R¹³, -CH=N-OCH₃ and



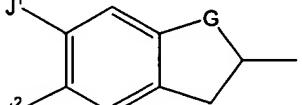
W is chosen from H, Cl, F, R⁸, C₁-C₄-alkylaryl, -OR⁸, -SR⁸, -NR⁹R¹⁰ and -NHC(O)R¹¹, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R⁸;

R¹ is chosen from alkyl, cycloalkyl, alkenyl, C₁-C₃-alkylcycloalkyl, heterocyclyl, C₁-C₃-alkylheterocyclyl, aryl, C₁-C₃-alkylaryl, heteroaryl, C₁-C₃-alkylheteroaryl, (C₁-C₃-alkyloxy)alkyl, (C₁-C₃-alkyloxy)cycloalkyl, (C₁-C₃-alkylthio)alkyl, (C₁-C₃-alkylthio)cycloalkyl and (C₁-C₃-alkylsulfonyl)alkyl;

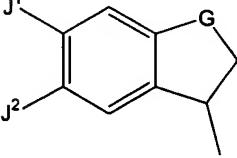
R^2 is H or C_1 - C_3 -alkyl, or R^1 and R^2 taken together form a 5- to 7-membered ring structure optionally containing O, S or NR^{12} ;

R^3 is H or C_1 - C_6 -alkyl, or, when n is zero, R^2 and R^3 taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R^4 is chosen from H, aryl, heteroaryl, C_1 - C_4 -alkyl substituted with from one to three aryl or heteroaryl residues,



and



, wherein J^1 and J^2 are independently chosen from H, F, Cl, CN, NO_2 and CH_3 , and G is chosen from $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-OCH_2-$, $-CH_2O-$, $-CH_2CH_2O-$, $-OCH_2CH_2-$, $-O-$, $-N(lower alkyl)-$, $-N(lower alkyl)CH_2-$, $-CH_2N(lower alkyl)-$, $-S-$, $-SO-$, $-SO_2-$, $-CH_2S-$, $-SCH_2-$, $-CH_2SO-$, $-SOCH_2-$, $-CH_2SO_2-$, and $-SO_2CH_2-$;

R^5 is H or C_1 - C_3 -alkyl, with the proviso that both R^3 and R^5 cannot be alkyl;

R^6 is aryl;

R^7 is aryl or C_1 - C_3 -alkylaryl;

R^8 is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C_1 - C_4 -alkylaryl, C_1 - C_4 -alkylheterocycl and C_1 - C_4 -alkylheteroaryl;

R^9 is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C_1 - C_4 -alkylcycloalkyl, (C_1 - C_4 -alkoxy)alkyl, (C_1 - C_4 -alkoxycarbonyl)alkyl, (C_1 - C_4 -alkylthio)alkyl, heterocycl, C_1 - C_4 -alkylheterocycl, C_1 - C_4 -alkylaryl, and C_1 - C_4 -alkylheteroaryl;

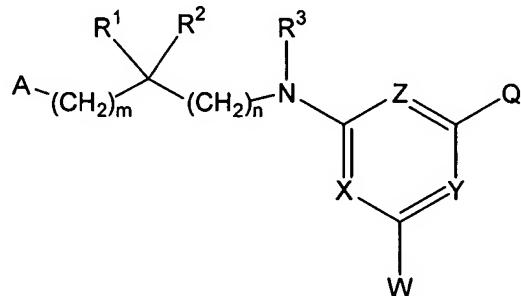
R^{10} is H or C_1 - C_3 -alkyl, or

R^9 and R^{10} taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO_2 or NR^{12} , said ring optionally substituted with $-OH$, $-CN$, $-COOH$ or $-COOCH_3$;

R^{11} is aryl;
 R^{12} is chosen from H, C₁-C₃-alkyl, alkoxy carbonyl, methoxyacetyl and aryl;
 R^{13} is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;
 m is zero or one; and

n is zero or one, with the proviso that when A is A², m and n cannot both be zero.

100. (previously added) A method of treating post-capillary resistance or diabetic symptoms associated with insulitis comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I



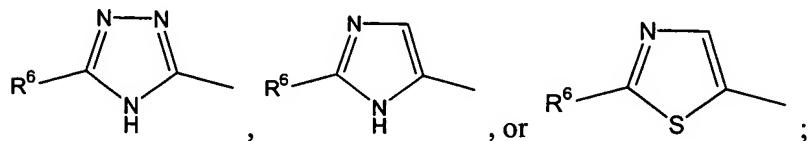
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wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

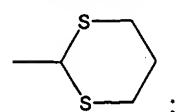
A is A¹ or A²;

A¹ is R⁴R⁵N-C(O)-,



A² is chosen from R⁷C(O)NH-, R⁷S(O)₂NH-, R⁴NH-, and R⁴O-;

Q is chosen from heteroaryl, aryl, -CH₂R¹³, -CH=N-OCH₃ and

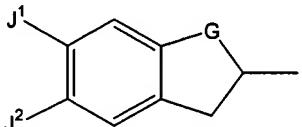
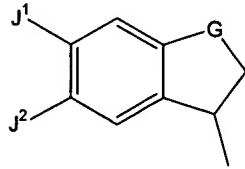


W is chosen from H, Cl, F, R⁸, C₁-C₄-alkylaryl, -OR⁸, -SR⁸, -NR⁹R¹⁰ and -NHC(O)R¹¹, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R⁸;

R¹ is chosen from alkyl, cycloalkyl, alkenyl, C₁-C₃-alkylcycloalkyl, heterocyclyl, C₁-C₃-alkylheterocyclyl, aryl, C₁-C₃-alkylaryl, heteroaryl, C₁-C₃-alkylheteroaryl, (C₁-C₃-alkyloxy)alkyl, (C₁-C₃-alkyloxy)cycloalkyl, (C₁-C₃-alkylthio)alkyl, (C₁-C₃-alkylthio)cycloalkyl and (C₁-C₃-alkylsulfonyl)alkyl;

R² is H or C₁-C₃-alkyl, or R¹ and R² taken together form a 5- to 7-membered ring structure optionally containing O, S or NR¹²;

R³ is H or C₁-C₆-alkyl, or, when n is zero, R² and R³ taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R⁴ is chosen from H, aryl, heteroaryl, C₁-C₄-alkyl substituted with from one to three aryl or heteroaryl residues,  and , wherein J¹ and J² are independently chosen from H, F, Cl, CN, NO₂ and CH₃, and G is chosen from -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -OCH₂-, -CH₂O-, -CH₂CH₂O-, -OCH₂CH₂-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH₂-, -CH₂N(lower alkyl)-, -S-, -SO-, -SO₂-, -CH₂S-, -SCH₂-, -CH₂SO-, -SOCH₂-, -CH₂SO₂-, and -SO₂CH₂-,

R⁵ is H or C₁-C₃-alkyl, with the proviso that both R³ and R⁵ cannot be alkyl;

R⁶ is aryl;

R⁷ is aryl or C₁-C₃-alkylaryl;

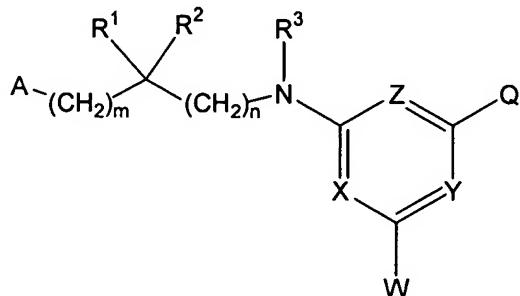
R⁸ is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C₁-C₄-alkylaryl, C₁-

C₄-alkylheterocycl and C₁-C₄-alkylheteroaryl;
R⁹ is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C₁-C₄-alkylcycloalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkoxycarbonyl)alkyl, (C₁-C₄-alkylthio)alkyl, heterocycl, C₁-C₄-alkylheterocycl, C₁-C₄-alkylaryl, and C₁-C₄-alkylheteroaryl;
R¹⁰ is H or C₁-C₃-alkyl, or

R⁹ and R¹⁰ taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with -OH, -CN, -COOH or -COOCH₃;

R¹¹ is aryl;
R¹² is chosen from H, C₁-C₃-alkyl, alkoxy carbonyl, methoxyacetyl and aryl;
R¹³ is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;
m is zero or one; and
n is zero or one, with the proviso that when A is A², m and n cannot both be zero.

101. (previously added) A method of treating edema comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I



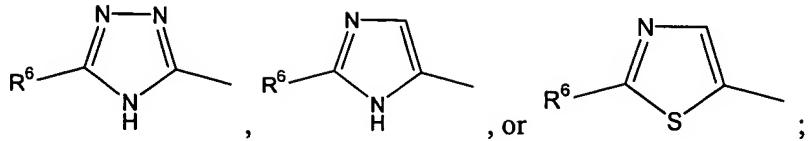
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wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

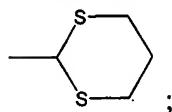
A is A¹ or A²;

A^1 is $R^4R^5N-C(O)-$,



A^2 is chosen from $R^7C(O)NH-$, $R^7S(O)_2NH-$, R^4NH- , and R^4O- ;

Q is chosen from heteroaryl, aryl, $-CH_2R^{13}$, $-CH=N-OCH_3$ and



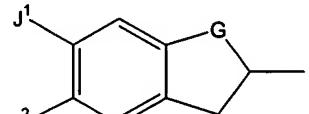
W is chosen from H, Cl, F, R^8 , C_1 - C_4 -alkylaryl, $-OR^8$, $-SR^8$, $-NR^9R^{10}$ and $-NHC(O)R^{11}$, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R^8 ;

R^1 is chosen from alkyl, cycloalkyl, alkenyl, C_1 - C_3 -alkylcycloalkyl, heterocyclyl, C_1 - C_3 -alkylheterocyclyl, aryl, C_1 - C_3 -alkylaryl, heteroaryl, C_1 - C_3 -alkylheteroaryl, (C_1 - C_3 -alkyloxy)alkyl, (C_1 - C_3 -alkyloxy)cycloalkyl, (C_1 - C_3 -alkylthio)alkyl, (C_1 - C_3 -alkylthio)cycloalkyl and (C_1 - C_3 -alkylsulfonyl)alkyl;

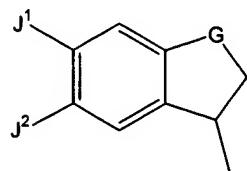
R^2 is H or C_1 - C_3 -alkyl, or R^1 and R^2 taken together form a 5- to 7-membered ring structure optionally containing O, S or NR^{12} ;

R^3 is H or C_1 - C_6 -alkyl, or, when n is zero, R^2 and R^3 taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R^4 is chosen from H, aryl, heteroaryl, C_1 - C_4 -alkyl substituted with from one to



three aryl or heteroaryl residues, and



, wherein J^1 and J^2 are independently chosen from H,

F, Cl, CN, NO₂ and CH₃, and G is chosen from -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -OCH₂-, -CH₂O-, -CH₂CH₂O-, -OCH₂CH₂-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH₂-, -CH₂N(lower alkyl)-, -S-, -SO-, -SO₂-, -CH₂S-, -SCH₂-, -CH₂SO-, -SOCH₂-, -CH₂SO₂-, and -SO₂CH₂-;

R⁵ is H or C₁-C₃-alkyl, with the proviso that both R³ and R⁵ cannot be alkyl;

R⁶ is aryl;

R⁷ is aryl or C₁-C₃-alkylaryl;

R⁸ is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C₁-C₄-alkylaryl, C₁-C₄-alkylheterocyclyl and C₁-C₄-alkylheteroaryl;

R⁹ is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C₁-C₄-alkylcycloalkyl, (C₁-C₄-alkoxy)alkyl, (C₁-C₄-alkoxycarbonyl)alkyl, (C₁-C₄-alkylthio)alkyl, heterocyclyl, C₁-C₄-alkylheterocyclyl, C₁-C₄-alkylaryl, and C₁-C₄-alkylheteroaryl;

R¹⁰ is H or C₁-C₃-alkyl, or

R⁹ and R¹⁰ taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO₂ or NR¹², said ring optionally substituted with -OH, -CN, -COOH or -COOCH₃;

R¹¹ is aryl;

R¹² is chosen from H, C₁-C₃-alkyl, alkoxy carbonyl, methoxyacetyl and aryl;

R¹³ is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is A², m and n cannot both be zero.